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Optimal and Individualized Pneumatic Calf Compression Pressure using Vekroosan to Improve Femoral Venous Flow Velocity in Patients with Severe Post Thrombotic Syndrome: Case Reports and Literature Review

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Abstract

Post thrombotic syndrome (PTS) symptoms usually occur after deep venous thrombosis (DVT) and eventually affects up to 50% of patients who have had a symptomatic DVT. Symptoms can include lower leg oedema, pain, changes in skin pigmentation, and venous ulcers. Severe PTS has a significant negative effect on quality of life. Thrombolytic therapy for acute DVT may decrease the risk of PTS, but carries its own risks. In patients with symptomatic proximal DVT, the use of knee-high compression stockings capable of exerting a pressure of at least 30 to 40 mmHg at the ankle and less at the knee has been found to be useful. There are practical difficulties in using these stockings and hence Intermittent Pneumatic Calf compression (IPC) devices are recommended. However not all devices have the capability to meet the requirements of mobile patients with severe PTS features. One such device was trialled on these patients to assess peak femoral flow velocity (PFV) and clinical benefits. There was mean 1.8 cm improvement in calf circumference measurements, post therapy and significant individual variations in achieving optimal femoral flow velocity. At a calf compression pressure of 40 mmHg, lower and upper chambers resulted in greater PFV in some patients and at 80 mmHg, middle and upper chambers achieved greater PFV in others. There was a significant variability noted in the PFV, although there was a uniform significant clinical benefit, hence the recommendation of individualising the calf compression pressures to meet the needs of these patients. This device appears to have addressed the needs of some of these patients.

Keywords: Post thrombotic syndrome; Programmed calf compression

Introduction

The post-thrombotic syndrome (PTS) is a complication of deep venous thrombosis (DVT) that is characterized by chronic, persistent pain, leg cramps or aches, swelling, changes in skin pigmentation, and venous ulcers. The management of patients with venous insufficiency as a result of PTS is similar to that of other patients with venous insufficiency. Up to half of patients with proximal DVT can develop variable degrees of PTS, despite optimal anticoagulant therapy [1]. PTS significantly impacts upon quality of life and has major health-economic implications. Recurrent thrombosis, thrombus location, history of varicose veins and obesity are major risk factors of PTS. Adequate anticoagulation and use of elastic compression stockings (ECS) following DVT can reduce the incidence of PTS. Catheter-directed thrombolysis and mechanical thrombectomy of acute DVT may preserve valvular function. Despite a large number of studies published in the literature, individual management of these patients remains a challenge. Calf compression therapy, aimed at reducing the underlying venous hypertension, remains the main stay of treatment to relieve some of the symptoms. This is despite a paucity of high-quality evidence to support its use [2]. There are various studies assessing calf compressors in patients with chronic venous disease and in healthy volunteers [3-7]. There is no clear data on optimal calf pressure and whether lower, mid or upper calf compression achieves best femoral flow velocity. This prompted our study in patients with PTS and our experience is described using a novel mobile sequential calf compressor device, VekroosanR (a patented product of DVT solution P/L), with a capacity to vary the individual chambers and hence individualize the therapy according to patients' needs [8].

We present a cohort study of patients with severe PTS features for an assessment of optimal calf compression required for an effective femoral venous flow and hence reduce symptoms of PTS. Calf compression stockings and bed/chair bound calf compression therapies had suboptimal outcomes in these patients due to either their inability to mobilize or modify pressure. Hence a mobile battery operated sequential calf compressor device, was used in these patients.

Aim

To assess optimal pressure sequencing of calf compression to improve femoral venous flow in patients with severe PTS, using a programmable, sequential and multi-chambered calf compression device, VekroosanR and the associated clinical benefits.

Methods

Patients with history of varicose veins, chronic venous disease symptoms, or chronic leg swelling following episode (s) of DVT and ongoing severe symptoms of PTS and unable to wear calf compression stockings for various reasons, were included in this study. Patients with acute DVT, acute pulmonary emboli, leg ulcerations or any open wound, severe peripheral arterial disease, history of malignancies requiring active chemotherapy, unable to consent or under the age of 18, were excluded. These patients were treated as outpatients in haematology clinics. Informed consent was obtained as per the ethics committees' requirement and study approval conditions.

Peak femoral venous velocity (PFV) measurements were performed using Doppler ultrasonography device, General Electric Logic S8. Colour doppler imaging with spectral doppler was used to demonstrate flow velocity rate and augmentation at external iliac, common femoral, distal superficial femoral and popliteal vein levels. VekroosanR was applied around patients' calf and the 3 chambers were inflated sequentially (Figure 2). The advantage of this device was that it was easy to apply without additional assistance from carers and patients can mobilise with the device. Furthermore, the pressures could be altered in each chamber individually, if required, to maximize the femoral flow velocity. External calf pressures could be altered depending on the individual tolerance and needs of the patient. Safety aspects of this device was tested and approved by an independent certifier, Austest AS/NZS CISPR 11 (approval no. 0119 DVT_RK-V16-7). Doppler recordings of PFV were performed using the doppler ultrasonography as above. Baseline pressure was recorded prior to applying the mobile calf compressor device and repeated pressure measurement at an average pressure of 60 mmHg and varied between 40-80 mmHg. Measurements at each time point where the average of five repeated determinations of the PFV. Measurements were performed after patients resting for 20-minute with the device inactive on the leg as a baseline measurement. Immediately after the device was turned on the measurements were repeated sequentially after activation of each chamber. The PFV measurements were performed for activation of chamber 1 (lower), chamber 2 (mid) and chamber 3 (upper) sequentially. The results were compared between baseline and post calf compression measurements, with lower, mid and upper chambers compressed, sequentially from lower to upper chamber. Calf circumference measurements were made at baseline and post calf compression (Figure 1). Other available models including Venopress (mobile), Arjo Huntleigh and Prius (non-mobile) calf compressors were either inappropriate or unsuitable for mobile patients, hence failed to meet the requirement for this cohort of patients with severe PTS symptoms.

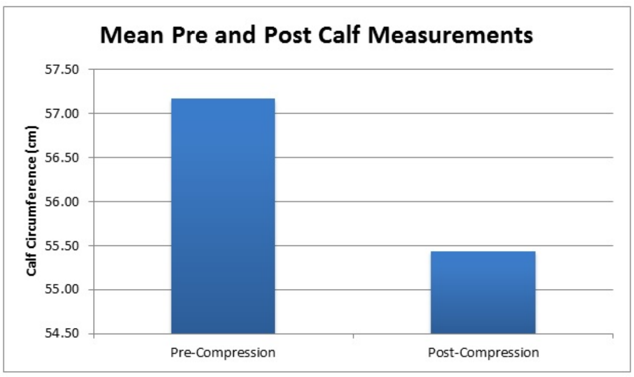

Figure 1: Pre and post compression calf circumference measurements.

Figure 2: VekroosanR device un-inflated (left) and inflated (right).

Statistical methods

Normality was assessed using the Shapiro-Wilks test. Differences in readings for calf compression pressure of 40 mmHg between baseline, lower, mid and upper settings was determined using a one-way repeated measures ANOVA. This was repeated for calf compression pressure of 80 mmHg. Mauchly's Test of Sphericity was used to test the assumption of sphericity. For calf compression pressure of 80 mmHg a Greenhouse-Geisser correction was applied as the assumption of Sphericity was not met (the variances of the mean differences between different settings was not equal). Mauchly's Test of Sphericity indicated that the assumption of sphericity was met for calf compression pressure of 40 mmHg ($\chi^2=5.63$, $p=0.34$) and not met for calf compression pressure of 80 mmHg ($\chi^2=20.17$, $p=0.001$). This was followed by post hoc analysis using the Bonferroni post hoc test for multiple comparisons. Results were considered statistically significant if $p<0.05$. All analyses were conducted in SPSS (version 23, SPSS, Chicago, IL, USA).

Results

There were 15 female and 8 male evaluable patients with a mean age of 68 (range 50-89 and SD 9.98). There was an increase in PFV pressure in post-compression measurement (Mean=11.92 cm/sec) (Table 1). Nine patients were able to complete Doppler PFV measurement in erect position with an increase in PFV (mean 2.35 cm/sec). There were no compliance or complications associated with the use of the device. All patients showed symptomatic benefit with the therapy, especially improved leg discomfort and pain. The device was used for up to 6 hours per day, averaging around 2 hours, especially when patients were mobile.

Calf circumference measurement improvement was noted in all patients. The mean pre and post circumferential calf measurements were 57.2 cm (± 9.6 cm) and 55.4 cm (± 9.4 cm), respectively (Range: 38-72 cm and 36.5-70.5 cm respectively). There was a statistically significant difference between pre and post circumferential calf measurements ($p<0.001$).

For calf compression pressure of 40 mmHg, the mean (± SD) baseline, lower, mid and upper readings were 19.0 cm (± 8.8 cm), 23.5 cm (± 10.8 cm), 22.9 cm (± 11.4 cm) and 22.9 cm (± 12.1 cm), respectively. For calf compression pressure of 40 mmHg, a repeated measures ANOVA determined that mean reading levels were statistically different between baseline, lower, mid and upper machine settings ($F=5.54$, $p=0.002$). Post hoc analysis indicated that reading values were significantly higher at lower ($p=0.002$) and upper ($p=0.038$) settings, than at baseline. However, post hoc analysis indicated that reading values were not significantly different between baseline and mid, lower and mid, lower and upper and mid and upper settings.

For calf compression pressure of 80 mmHg, the mean (± SD) baseline, lower, mid and upper readings were 19.1 cm (± 8.8 cm), 23.7 cm (± 12.4 cm), 24.5 cm (± 11.3 cm) and 27.0 cm (± 17.1 cm), respectively. For calf compression pressure of 80 mmHg, a repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean reading levels were statistically different between baseline, lower, mid and upper machine settings (F=5.09, p=0.011). Post hoc analysis indicated that reading values were significantly higher at mid (p=0.016) and upper (p=0.032) settings, than at baseline. However, post hoc analysis indicated that reading values were not significantly different between baseline and lower, lower and mid, lower and upper and mid and upper settings.

Case no.	Age/Sex	History	Doppler study	Calf measurements (pre/Post) (cms)	Comments
1	89/M	Left calf DVT	Chronic venous insuffiency changes	58/54	Better increment with lower pressure erect position
2	83/F	Right Calf and previous PE	Minor varicosities	62/60.5	Higher pressure/middle cuff had a slight advantage
3	61/M	Recurrent left superficial and deep venous thrombosis.	Persisting non occlusive LSV thrombus	49.5/48	Lower pressure and lower cuff produced best results
4	78/F	Left calf DVT/PE	Chronic changes seen	64/61.5	Lower pressure upper cuff achieved better increment
5	78/F	Right calf	Minor changes	56/54	Higher pressure lower cuff better
6	70/F	Recurrent DVT	Chronic changes seen	63.5/61	Lower pressure lower cuff better flow velocity
7	82/F	Recurrent superficial and DVT	Chronic changes seen	70/67	Lower pressure lower cuff better flow velocity
8	60/F	Recurrrent DVTs	Chronic changes seen	59.5/57.5	Lower pressure lower cuff better flow velocity
9	60F	Recurrent calf DVT	Minor chronic changes	48/47	Lower pressure mid cuff better flow velocity
10	69F	Left proximal DVT	Chronic changes and varicose veins	56.5/54	Lower pressure mid cuff better flow velocity
11	61 M	Left DVT	Old LSV Thrombosis	62/61	Lower/mid cuff at any pressure best suited
12	74/M	Left DVT	Chronic venous changes	58.5/56	Lower chamber at higher pressure showed best results
13	76/F	Right DVT	Varicosities and non-occlusive changes	61/59	Middle chamber at higher pressure in supine and lower chamber in supine position at lower pressure showed best results
14	68/M	Right DVT	Minor varicosities	49/48	Lower and upper chambers at higher pressure in supine and lower chamber in erect position at lower pressure showed best results
15	71/F	Right DVT (SFV)	Chronic venous changes	72/70.5	Middle chamber at higher pressure in supine and upper chamber at lower pressure in erect position showed best results. Maoderate oedema
16	71/M	Left DVT	Persisting non occlusive LSV thrombus and varicosities	69/68.5	Middle chamber at higher pressure in supine and lower chamber in erect position at lower pressure showed best results
17	64/F	Right DVT	Chronic venous changes	48/47	Lower chamber at higher pressure in supine and in erect position showed best results
18	64/F	Left DVT (SFV)	Chronic venous changes and varicosities	53/51.5	Upper chamber at higher pressure in supine position showed best results
19	51/M	Right DVT	No major persisting abnormalities	47/46	Lower chamber at higher pressure in supine and middle chamber in erect position at lower pressure showed best results
20	50/F	Right DVT	Chronic venous changes and varicosities	53/51.5	Upper and lower to a lesser degree, chambers at higher pressure in supine showed best results

21	54/F	Right DVT	Chronic venous changes	66/65	Lower chamber at higher pressure in erect position at lower pressure showed best results. Overall, little difference.
22	62/M	Right proximal DVT	Chronic venous changes	42.5/41	Middle chamber at higher pressure in supine and lower chamber in erect position at lower pressure showed best results
23	69/F	Left DVT	Persisting non occlusive thrombus	47/45.5	Upper chamber at higher pressure and middle chamber at lower pressure showed best results

Table 1: Complete Doppler PFV measurement in erect position.

Discussion

External calf pressure variability

Calf compression therapy is an important part of treatment of patients with PTS to reduce related complications 5. PTS or Chronic venous disease (CVD) of the lower limbs is caused by abnormalities of the venous wall and valves that leads to obstruction or reflux of blood flow in the veins [9]. The calf can become permanently enlarged and hard, and venous ulcers occur more frequently and often difficult to heal [10]. Consequently, it adds to the individual's suffering and morbidity and hence significant burden to the health care system. The direct and indirect costs of chronic venous disease or PTS have been estimated at three billion U.S. dollars per annum [7]. Sustained calf compression is an important part of chronic venous leg ulcer therapy, to promote ulcer healing and prevent recurrence. This has been used as the basis for preventative measures in patients with PTS using calf compression stockings, which can be very difficult to wear. To date, there are no published data on the use of individualized calf compression therapy. This prompted our study using individualized mobile sequential pneumatic calf compression therapy.

In this cohort of elderly patients with severe PTS, 83% of patients showed significant femoral blood flow improvement with external calf compression device and in the majority of evaluable patients, even when examined in an erect position. All patients showed symptomatic improvement in terms of leg swelling and associated pain. This may be due to improved flow in these patients with venous insufficiency and varicosities secondary to DVT that leads to valve dysfunction and hence reflux of blood flow in the 'wrong' direction if not appropriately programmed. There appears to be a 'balooning' effect if upper chambers are overinflated. There was significant immediate benefit of leg swelling and hence relief from lower limb pain and discomfort after calf compression therapy. Post hoc analysis at a lower calf compression pressure (40 mmHg) indicated that reading values were significantly higher at lower ($p=0.002$) and upper ($p=0.038$) settings, than at baseline and that reading values were significantly higher at mid ($p=0.016$) and upper ($p=0.032$) settings, than at baseline in other patients who required 80 mm Hg calf compression pressure. Therefore, individualizing the pressure of calf compression is recommended to achieve clinical benefits, which were not demonstrated in previous published studies described below. The data shows that single chamber or one fixed pressure across multiple chambers is unlikely to achieve optimal femoral flow and the expected clinical benefits and hence the therapy needs to be individualised to suite the patient's needs.

Clinical and symptomatic benefits

Previous studies have shown that use of IPC leads to improvement of leg swelling and associated pain in patients with chronic PTS or patients undergoing orthopedic or spinal surgery. 6 However, there are no large studies to substantiate its use and the utility of mobile IPC for the management of advanced chronic venous disease, deep venous thrombosis (DVT) and patients having undergone high-risk surgical procedures for thrombosis such as joint replacement surgeries and abdominal and pelvic surgeries. Often patients do not comply with compression therapies, such as stockings, bandages, and non-mobile IPC units because of difficulty with use of these therapies [7]. The use of IPC in patients with DVT or PTS has been discussed in a review of its application [9]. It was concluded by the author and further supported by relevant literature that the full potential of IPC devices has probably not yet been realized, and requires better quality research. System design must follow physiological evidence, and while complexity in that design may allow greater therapeutic flexibility, it may incur greater financial cost, difficulty in use, and in particular, may be unnecessary in the prevention of DVT [10]. Studies have shown improved PFV measurements in volunteers that are statistically significant with a fivefold increase, relative to baseline [11,12]. This increase in PFV is consistent with increases reported by others, for IPC devices, with a flow velocity of 35–60 cm/sec [12-14]. Hence, there is evidence that increased PFV is considered to be one of the possible mechanisms of thrombosis prophylaxis. Furthermore, in a large prospective study of patients with an initial venographically confirmed DVT, the cumulative incidence of postphlebitic changes at one, two, and five years was 17, 23, and 28%, respectively; the numbers did not increase there after [15]. The incidence of severe changes of chronic venous insufficiency, including venous ulcer, increased from 2.6% at one year to 9.3% at five years. However, clinical and symptomatic benefit has not always been substantiated, which has been addressed in this study.

Elastic compression stockings to prevent PTS has been the mainstay of therapy in patients with PTS to prevent further thrombotic events, but post-operative mechanical calf compression in orthopedic patients, after the initial period of anticoagulation therapy has been found to be useful. 12 A randomized trial by Kahn et al has shown that the compression stockings do not prevent PTS after first proximal DVT [16]. There was also evidence that significant number of patients with proximal DVT do go on to develop PTS. 2 This can occur despite adequate anticoagulation therapy. Hence management of these patients post-DVT in terms of reducing their long-term consequences of PTS remains a challenge. In recent times there has been a number of intermittent pneumatic calf compression devices available to reduce this risk of PTS, or DVTs [17-19]. However, there has been no conclusive evidence, or large clinical trials in post-op patients, patients with PTS, or chronic venous insufficiency to recommend any specific device. In our study, calf circumference measurement improvement was noted in all patients. The mean pre and post circumferential calf measurements were 57.2 cm (± 9.6 cm) and 55.4 cm (± 9.4 cm), respectively (Range: 38-72 cm and 36.5-70.5 cm respectively). There was a statistically significant difference between pre and post circumferential calf measurements ($p<0.001$). All patients reported symptomatic relief with reduced leg swelling and discomfort, demonstrating the clinical and symptomatic benefits associated with the use of such devices as VekroosanR.

Our study has refined the use of an IPC that can be modified to an individual's needs that allows mobilization whilst undergoing calf compression, using a battery operated programmable sequential calf compression device without any power cords or restriction of movement. This study highlights the need to individualize the calf pressure to improve the venous return and hence reduce associated symptoms of venous hypertension. The 'one-size fits all' approach unfortunately does not help all patients and this study has validated that pressure variations to suit the needs of individual patients are warranted. Hence, devices that has no capability to vary pressures or multiple chambers for appropriate sequencing cannot be recommended. This device appears to have the necessary capacity to vary the chamber pressure to optimize the flow of these patients and consequently significant flow improvement. Larger studies are required to confirm our findings but this case series highlights the need for improved mechanical devices and therapy to improve quality of life in these patients who cannot use calf compression stockings or mobility limited by power source of IPC devices. Although our study has addressed and shown clinical benefits in patients with severe PTS, there is a need for extending its use post-operatively to reduce the risk of DVTs and associated morbidities. Furthermore, comparative studies with other devices and combination with pharmaceutical thrombo-prophylactic therapies are also required to further validate our findings.

Conclusion

Post Thrombotic syndrome can be a sequel of DVT in around 30-50% of patients and proximal DVT, varicose veins, obesity and other medical issues appear to increase this risk. Patients with PTS are prone to significant morbidities and hence a major health cost to the medical system. A novel calf compression device, VekroosanR has shown a major step forward in managing these patients. This cohort case study has shown significant clinical benefit both in terms of achieving PFV increment, reduction in calf circumference and potentially improved compliance with the ease of its use.

Calf compression therapy to reduce the venous hypertension and hence reduce risk of further thrombotic event and post-thrombotic syndrome symptoms remains a mainstay of therapy. Further studies are warranted to substantiate its use. Individualising the calf compression pressure is highly recommended based on our observation.

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